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1	Substitute	for form 1449A/PTC)		i	Complete if Known
ı					Application Number	10/579,251
ı	INFO	RMATION	DIS	CLOSURE	Filing Date	October 20, 2006
ı	STAT	EMENT B	Y AI	PPLICANT	First Named Inventor	Luca Gianni
ı					Art Unit	1623
L		(Use as many she	ets as	necessary)	Examiner Name	Jonathan S. Lau
7	Sheet	1	of	5	Attorney Docket Number	13566.105020

			U.S. PATE	NT DO	CUME	ENTS		
Examiner	Cite	Document Number	Publication D	Date (Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevan	
Initials *	No.1	Number - Kind Code ² (if known)	MM-DD-YY	YY			Passages or Relevant Figures Appear	
		US- 20040108086	06/10/200	04		'akahashi et al.		
		US- 20040002602	01/01/04	1	F	rancesch et al.		
		US- 5,149,804	9/22/199	2		Rinehart et al.		
		US- 5,654,426	8/5/1997	7		Rinehart et al.		
		US- 5,721,362	2/24/199	/1998 Corey et al.				
		US- 5,908,835	06/01/199	99	Bissery Rinehart et al. Rinehart et al. Cuevas et al.			
		US- 5,985,876	11/16/199	99				
		US- 6,124,293	9/26/200	0				
		US- 7,241,892	07/10/07	7				
		F	OREIGN PA	TENT	DOCU	MENTS	A	
Examiner	Cite	Foreign Patent Document			cation	Name of Patentee or	Pages, Columns, Lines,	
Initials*	No.1	Country Code ³ - Number ⁴ - Kind I	Code ⁵ (if known)	D	ete D-YYYY	Applicant of Cited Document	Where Relevant Passages or Relevant Figures Appear	T ⁶
		WO 00/6986	2	11/23	3/2000	Cuevas et al.		
		WO 01/7711	5	10/18	3/2001	Flores et al.		
		WO 01/87894	1	11/22	2/2001	Cuevas et al.		

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		Burstein et al., "Phase I study of Doxil and Vinorelbine in Metastatic Breast Cancer," Annals of Oncology, vol. 10, pages 1113-1116, 1999, XP8086751	
		Delaloge et al., "Ecteinascidin (ET-743) in heavily pretreated refractory sarcomas: Preliminary evidence of activity," Eur. J. Cancer, vol. 35, suppl. 4, page S271, Abstract No. 1080, Sept 15, 1999	
		D'Incalci et al., "Mode of action of Ecteinascidin-743 (ET-743)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, pages 3872s-3873s, Abstract of Plenary Session 7, November 16-19, 1999	
		European Medicines Agency (EMEA), "Scientific Discussion" from the European Public Assessment Report for Yondelis®, Revision 1, published March 31, 2008, downloaded from the internet on April 2, 2008, from the website < http://www.emea.europa.eu/humandocs/Humans/EPAR/yondelis/yondelis.htm">http://www.emea.europa.eu/humandocs/Humans/EPAR/yondelis/yondelis.htm	
		Faulkner et al., "Symbiotic Bacteria in Sponges: Sources of Bioactive Substances," Drugs from the Sea, Fusetani, N. (ed.), Basel Karger, 2000, pp. 107-119	
		Garcia-Carbonero et al., "Population pharmacokinetics of ecteinascidin 743 in patients with advanced soft tissue sarcoma," Clinical Cancer Research, vol. 6, Supplement, Abstract 211, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
		Giovanna et al., "Importance of DNA repair mechanisms for the sensitivity of tumor cells to ET-743," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 303, November 16-19, 1999	
		Gore et al., "Phase I Combination Study of Trabectedin and Capecitabine in Patients With Advanced Malignancies," Poster Presentation, 42nd ASCO Annual Meeting held on June 2-6, 2006, Atlanta, Georgia	
		Hahn et al., "Taxol in Combination with Doxorubicin or Etoposide," CANCER, vol. 72, no. 9, pp. 2705-2711, November 1, 1993	
		Hornicek et al., "In vitro effect of the tetrahydroisoquinoline alkaloid Ectelnascidin-743 (ET-743) on chondrosarcoma (CHSA) cells," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 304, November 16-19, 1999	
		Jimeno et al., "Pharmacokinetics (PK)/Pharmacodynamic (PD) Relationships in Patients (PT) Treated With Ecteinascidin-743 (ET-743) Given As 24 Hours Continuous Infusion (CI)," Journal of Clinical Oncology, ASCO Annual Meeting Proceedings, Abstract No. 744, May 15-18, 1999	

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)
Sheet 3 of 5

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		Jin et al., "The antitumor agent Ecteinascidin 743 (ET743), inhibits transcriptional activation of the MDR1 Gene by multiple inducers," Proceedings of the 1999 AACR-NOI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 302, November 16-19, 1999	
		Kovalcik et al., "The Stability of Cyclophosphamide in Lyophilized Cakes. part I. Mannitol, Lactose, and Sodium Biocarbonate as Excipients," Journal Farenteral Science and Technology, vol. 42, no. 1, Jan-Feb. 1988, pp. 29-37	
		Lopez-Lazaro et al., "Exploratory evaluation of the potential predictors for dose- limiting toxicities (DLTs) in patients treated with Ecteinascidin-743 (ET-743) as a 24-h intravenous (N) influsion every 3 weeks and its relationship to pharmacokinetics (PK)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s., Abstract 308, November 16-19, 1999	
		Lyass et al., "Phase I Study of Doxil-Cisplatin Combination Chemotherapy in Patients with Advanced Malignancies," Clinical Cancer Research, vol. 7, pages 3040-3046, October 2001, XP806675.	
		Manzanares et al., "Advances in the Chemistry and Pharmacology of Edelinascidins, A Promising New Class of Anticancer Agents," Curr. Med. Chem Anti-Cancer Agents, 2001, vol. 1, pp. 257-276	
		Menchaca et al., "Synthesis of Natural Ecteinascidins (ET-729, ET-745, ET-7598, ET-736, ET-637, ET-694) from Cyanosafracin B," J. Org. Chem., published on web October 21, 2003, pp. 8859-8866	
		Rosing et al., "Pharmacokinetics (PK) of Ecteinascidin-743 (ET-743) in three different phase I trials," Proceedings of the American Association for Cancer Research, vol. 40, pp 81, abstract no. 542, March 1999	
		Ryan, D.P. "Studies with Ecteinascidin-743 (ET-743) A Marine Alkaloid," Cancer Invest, vol. 18 (suppl 1), pp 112, abstract no. 87, January 2000, from the Chemotherapy Foundation Symposium XVII Innovative Cancer Therapy for Tomorrow, November 3-6, 1999, New York, NY	
		Sakai et al., "Additional Antitumor Ecteinascidins from a Caribbean Tunicate: Crystal Structures and Activities in vivo," Proc. Natl. Acad. Sci., vol. 89, Dec. 1992, pp. 11456-11460	
		Scotto et al., "Ecteinascidin 743, a novel chemotherapeutic agent that targets transcriptional activation of a subset of genes, including MDR1," Clinical Cancer Research, vol. 6, Supplement, Abstract 210, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
		Shertzer et al., "Protection Against Carbon Tetrachloride Hepatoxicity by Pretreatment with indole-3-carbinol," Exptl. Molec. Pathol., vol. 46, pp. 180-189 (1987)	

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE
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(Use as many sheets as necessary)
Sheet 4 of 5

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		Shertzer et al., "Protection from N-Nitrosodimethylamine Mediated Liver Damage by Indole-3-carbinol," Exptl. Molec. Pathol., vol. 47, pp. 211-218 (1987)	
		Taamma, A. et al., "Ecteinascidin-743 (ET-743) 24 hours continuous infusion (CI): clinical and pharmacokinetic phase I study in solid tumor patients (PTS). Preliminary Results" 1998 ASCO Annual Meeting Proceedings, Abstract No. 890, 1998	
		Taamma et al., "Ecteinascidin-743 (ET-743) 24 hour continuous intravenous infusion (CI) phase I study in solid tumors (ST) patients (pts)." Proceedings of the American Association for Cancer Research , vol. 39, pp 323, abstract no. 2207, March 1998	
		Taamma et al., "Ecteinascidin-743 (ET-743) in heavily pretreated refractory sarcomas: early results of the French experience," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s, Abstract 309, November 16-19, 1999	
		Takebayashi et al., "Multidrug Resistance Induced by DNA Minor Groove Alkylation of Ecteinascidin 743 (E1743)," Proceedings of the 1999 AACR-NCI- EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3851s, Abstract 602, November 16-19, 1999	
		Takebayashi et al., "Nucleotide excision repair-dependent cytotoxicity of Ecteinascidin 743," Clinical Cancer Research, vol. 6, Supplement, Abstract 207, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Th	
		Takahashi et al., "Sequence-dependent Synergistic Cytotoxicity of Ecteinascidin-743 and Pacilitaxel in Human Breast Cancer Cell Lines in Vitro and in Vivo," Cancer Research, 62: 6909-6915 (Dec. 1, 2002)	
		Ten Hagen et al., "Pegylated Liposomal Tumor Necrosis Factor-Alpha Results in Reduced Toxicity and Synergistic Antitumor Activity after Systemic Administration in Combination with Liposomal Doxorubicin (Doxil) in soft tissue Sarcoma-Bearing Rats," Int. J. Cancer, vol. 97, pages 115-120, 2002	
		Twelves et al., "Phase I Trials with ET-743, a marine derived (MD) anticancer agent," Eur. J. Cancer, vol. 35, suppl. 4, page S283, Abstract No. 1135, Sept 15, 1999	
		van Kesteren et al. "Clinical Pharmacology of the Novel Marine-derived Anticancer Agent Ecteinascidin 743 Administered as a 1- and 3-h Infusion in a Phase I Study," Anti-Cancer Drugs, Vol. 13, No.4, pgs. 381-393, April 2002	
		Weiwei et al., "Potent antitumor activity of ET-743 against human soft tissue sarcoma cell lines," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 305, November 16-19, 1999	

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		Zelek et al., "Preliminary results of phase II study of ecteinascidin (ET-743) with the 24 hour (H) continuous infusion (CI) q3week schedule in pretreated" Clinical Cancer Research, vol. 6, Supplement, Abstract 212, pages 4508s-4509s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000				

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